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EXAMINER

KAM, CHIH MIN

ART UNIT

PAPER NUMBER

1653

DATE MAILED: 09/24/2002

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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/493,211

Applicant(s)

APPELMELK ET AL.

Examiner

Chih-Min Kam

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 08 July 2002.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1,3-23,26-40 and 42-50 is/are pending in the application.
- 4a) Of the above claim(s) 14 and 31-39 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1,3-13,15-23,26-30,40 and 42-50 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.
- If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
- a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- 1) ☐ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____.
- 4) ☐ Interview Summary (PTO-413) Paper No(s). _____.
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other: _____.

DETAILED ACTION

Oath/Declaration

1. The oath or declaration is defective. A new oath or declaration in compliance with 37 CFR 1.67(a) identifying this application by application number and filing date is required. See MPEP §§ 602.01 and 602.02. The oath or declaration is defective because: the instant application claims entering the national stage in the oath, while it is a continuation-in-part of PCT/NL 97/00449 filed July 31, 1997 as indicated in the preliminary amendment (Paper No. 5).

Status of the Claims

2. Claims 1, 3-23, 26-40 and 42-50 are pending.

Applicants' amendment filed July 8, 2002 (Paper No. 17) is acknowledged, and applicants' response has been fully considered. Claims 1, 3, 4, 8-12 and 15 have been amended, claims 2, 24, 25 and 41 have been cancelled, and new claims 48-50 have been added. Claims 14 and 31-39 stand withdrawn from consideration because they are non-elected invention. Thus, claims 1, 3-13, 15-23, 26-30, 40 and 42-50 are examined.

Rejection Withdrawn

Claim Rejections - 35 USC § 112

3. The previous rejection of claims 2, 4, 8-12, 15, 24, 25 and 41 under 35 U.S.C.112, second paragraph, regarding insufficient antecedent basis in claim 4, the term "having" in claims 8-12, and duplicate claims for claims 15, 24, 25 and 41, is withdrawn in view of applicants' amendment to the claim, applicants' cancellation of the claim, and applicants' response at pages 5-6 in Paper No. 17.

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Objection to New Matter Added to Specification

4. The supplemental amendment filed April 22, 2002 (Paper No. 11) is objected to under 35 U.S.C. 132 because it introduces new matter into the disclosure. 35 U.S.C. 132 states that no amendment shall introduce new matter into the disclosure of the invention. The added material which is not supported by the original disclosure is as follows: The specification does not indicate a purified peptide comprising at least 12 amino acids, being amphipathic, cationic and forming stable α -helix, and having the formula (I), $R^1_a-R^2_b-A-B-X_m-C_n-R^3_c$, where X is (A-C-B-A); a pharmaceutical composition comprising the peptide; a method for treating microbial infection comprising administering the peptide; and a method of for inhibiting the growth of a microbe comprising administering the peptide, however, the new claim (claims 1) in the amendment recites the new matters.

Applicant is required to cancel the new matter in the reply to this Office Action.

Claim Rejections - 35 USC § 101

35 U.S.C. 101 reads as follows:

Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

5. Claims 8-12 are rejected under 35 U.S.C. 101 because the claimed invention is directed to non-statutory subject matter. The claim is drawn to a peptide comprising SEQ ID Nos:1, 2, 3, 4 or 5. As written, the claim does not explicitly indicate the hand of man. Insertion of "synthetic" or "purified" in connection with a peptide is suggested. See MPEP § 2105.

In response, applicants indicate the claimed peptides are synthetic peptides, not derived from an organism, and "purified" is only used to refer naturally occurring proteins. The argument is not found persuasive because either a synthetic or naturally occurring peptide can be

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purified during the process of synthesis or isolation. Therefore, the addition of the term “synthetic” or “purified” in connection with peptide would indicate the hand of man.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

6. Claim 1, 3-7, 13, 15-23, 26-30, 40 and 42-50 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claims 1, 3-7, 13, 15-23, 26-30, 40 and 42-50 are directed to a peptide comprising at least 12 amino acids, being amphipathic, cationic and forming stable α -helix, and having the formula (I), $R^1_a-R^2_b-A-B-X_m-C_n-R^3_c$, where X is (A-B-C-A) or (A-C-B-A); a pharmaceutical composition comprising the peptide; a method for treating microbial infection comprising administering the peptide; and a method of for inhibiting the growth of a microbe comprising administering the peptide. The specification indicates a formula of peptides, $\{R_1-R_2-A_1-B_1-(A_2-B_2-C_1-A_3)_m-(C_2)_n-R_3\}$ has either the orientation according to the formula or the retro orientation thereof, wherein at least 0-m of the repetitive sequence motifs (A₂-B₂-C₁-A₃) have the retro orientation and the remaining repetitive motifs (A₂-B₂-C₁-A₃) have the orientation as presented in the formula (page 10, lines 15-26). However, the specification does not describe a formula of peptides, $\{R_1-R_2-A_1-B_1-(A_2-B_2-C_1-A_3)_m-(C_2)_n-R_3\}$ have only the retro orientation (A-C-B-A), and there is no disclosure indicating the making and use of these peptides. The specification

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only demonstrates the antimicrobial effects of several amphiphilic cationic peptides such as BP1, BP2, BP2.3, BP2.4 and BP2.5 which have both (A-B-C-A) and (A-C-B-A) motifs in the sequences (page 12, lines 19-28). Without guidance on identities of peptides containing retro orientation (A-C-B-A), one skilled in the art would not know how to make and/or use these peptides. Because of the lack of description on the identities and effects of peptides of formula (I) containing (A-C-B-A), applicants have failed to sufficiently describe the claimed invention, in such full, clear, concise terms that a skilled artisan would not recognize applicants were in possession of the claimed invention.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

7. Claims 5, 6, 42 and 48 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 5 recites the limitation “R¹-R²” in line 1. There is insufficient antecedent basis for this limitation in the claim because claim 1 only recites “R¹_a-R²_b” in the claim, not “R¹-R²”.

Claim 6 recites the limitation “motifs (A-C-B-A) are present in said peptide in a greater amount than motifs (A-B-C-A)” in lines 1-2. There is insufficient antecedent basis for this limitation in the claim because claim 1 defines X is either (A-B-C-A) or (A-C-B-A), the formula (I) does not contain both (A-B-C-A) and (A-C-B-A) motifs.

Claim 42 recites the limitation “x and y are each 0” in line 1. There is insufficient antecedent basis for this limitation in the claim.

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Claim 48 recites the limitation " R^2 is ACAA" in line 1. There is insufficient antecedent basis for this limitation in the claim because claim defines R^2 is an amino acid, thus, $R^2_{b=4}$ can only be AAAA, and R^2 cannot be a peptide of ACAA.

In response to previous rejection of claims 1-13, 15-30 and 40-47 under 35 U.S.C. 112, second paragraph, regarding (i) the Formula (I) is not reflected in the written part of claim 1 describing the formula in claim 1; (ii) the dependent claims are not consistent with the formula; and (iii) the comparison of amino acid sequences of BP1 (SEQ ID NO:1), BP-2 (SEQ ID NO:2), BP2.3 (SEQ ID NO:3), BP2.4 (SEQ ID NO:4) and BP2.5 (SEQ ID NO:5) with formula (I) shows that these sequences do not conform to formula (I), applicants have amended claims 1 and 3-6. The response has been considered, but it is not fully persuasive because of the following reasons:

As to point (i), the formula (I) has been amended to indicate the motif may be present in either (A-B-C-A) or (A-C-B-A), but, not both. After the amendment, the Formula (I) is reflected in the written part of claim 1 describing the formula, however, the peptide of formula (I) may contain only (A-C-B-A) motif, which is not described in the specification (See the rejection under 35 U.S.C. 112, first paragraph, and objection to new matter).

As to point (ii), claims 1 and 4 have been amended, and claim 4 is consistent with the limitation cited in claim 1, however, claims 5, 6, 42 and 48 are not (See the rejection under 35 U.S.C. 112, second paragraph, shown above).

As to point (iii), the amino acid sequences of BP1 (SEQ ID NO:1), BP-2 (SEQ ID NO:2), BP2.3 (SEQ ID NO:3), BP2.4 (SEQ ID NO:4) and BP2.5 (SEQ ID NO:5) do not conform to formula (I) because peptides of formula (I) may contain (A-B-C-A) or (A-C-B-A), but, not both

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as indicated in the amended claim 1. However, BP1, BP-2, BP2.3, BP2.4 and BP2.5 contain both (A-B-C-A) and (A-C-B-A) motifs. Applicants indicate, for example, $BP1 = R^1_{a=2}-R^2_{b=3}-A-B-X_{m=2}-C_{n=3}-R^3_{c=1}$ (page 7 of the response), where R^1 are Gly and Arg; R^2 are Leu, Arg and Lys; A is Lys; B is Trp; X are Lys-Ala-Phe-Lys and Lys-Phe-Leu-Lys; C are Ile, Leu and Ala; and R^3 is Gly. The comparison of BP1 to the formula (I) made by applicants is not correctly described, e.g., R^1_2 means R^1-R^1 , which can only be Gly-Gly or Arg-Arg, not Gly-Arg; $X_{m=2}$ can only be (A-B-C-A)₂ or (A-C-B-A)₂, not (A-B-C-A)-(A-C-B-A), the same rule is also applied to R^2_b , C_n and R^3_c . Therefore, the amino acid sequence of BP1 does not conform formula (I).

8. Claims 1, 3-7, 13, 15-23, 26-30, 40 and 42-50 are indefinite because of the use of the term “ R^1 , R^2 and R^3 are each an amino acid and may be the same or different”. The term “ R^1 , R^2 and R^3 are each an amino acid and may be the same or different” renders the claim indefinite, it is unclear what peptide is intended for the formula (I), e.g., which amino acid is used as R^1 , R^2 and R^3 . Claims 3-7, 13, 15-23, 26-30, 40 and 42-50 are included in the rejection for being dependent of a rejected claim and not correcting the deficiency of the claim from which they depend.

In response, applicants indicate R^1 , R^2 and R^3 are limited to 0-15 amino acids, and R^1 , R^2 and R^3 can be any amino acid as indicated in the specification (page 8 of the response). The argument is not found persuasive because the claim does not clearly indicate which amino acid is used as R^1 , R^2 and R^3 , therefore, it is not clear what amino acid sequence the peptide of formula (I) has.

Conclusion

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9. No claims are allowed.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire **THREE MONTHS** from the mailing date of this action. In the event a first reply is filed within **TWO MONTHS** of the mailing date of this final action and the advisory action is not mailed until after the end of the **THREE-MONTH** shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than **SIX MONTHS** from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Chih-Min Kam whose telephone number is (703) 308-9437. The examiner can normally be reached on 8.00-4:30, Mon-Fri.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christopher Low, Ph. D. can be reached on (703) 308-2923. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 308-0294 for regular communications and (703) 308-4227 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

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Chih-Min Kam, Ph. D.
Patent Examiner

CMK

September 19, 2002

Karen Cochrane Carlson Ph.D.
KAREN COCHRANE CARLSON, PH.D.
PRIMARY EXAMINER